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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/171,432	11/23/1998	HOWARD A. FIELDS	03063-0231US	8029
23859	7590	12/02/2003	EXAMINER	
NEEDLE & ROSENBERG, P.C. SUITE 1000 999 PEACHTREE STREET ATLANTA, GA 30309-3915			LUCAS, ZACHARIAH	
			ART UNIT	PAPER NUMBER
			1648	38
DATE MAILED: 12/02/2003				

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/171,432

Applicant(s)

FIELDS ET AL.

Examiner

Zachariah Lucas

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 September 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,69-71 and 73-89 is/are pending in the application.
- 4a) Of the above claim(s) 1, 69, 73-76, 79-82 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 83-89 is/are allowed.
- 6) ☒ Claim(s) 70,71,77 and 78 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

## DETAILED ACTION

### *Status of the Claims*

1. Claims 1, 69-71, 73-89 are currently pending in the present application. Claims 70, 71, 77, 78, and 83-89 are under consideration to the extent that they read on embodiments wherein the isolated, antigenically reactive hepatitis A virus (HAV) peptide comprises a portion of the HAV P2A protein, or conservative variations thereof. Claims 1, 69, 73-76, and 79-82 have been withdrawn as to non-elected inventions.

Claims 70-72, 77, and 78 were rejected in the prior Office Action, mailed on April 8, 2003 (the prior action). The Applicant has amended claims 70, 71, 77, and 78 in the Response filed on September 11, 2003 (the Response). Also, new claims 83-89 have been added to the application.

2. It is noted that claim 1 has not been indicated as pending by either the Applicant or the Office in the papers filed after the Applicant's filing of the response of April 2002 (dated Feb. 2002), which paper indicated that the claim was withdrawn and not cancelled. After this date, all papers appear to indicate that claim 1 was cancelled from the Application. However, it is not clear whether this claim was canceled. Clarification of the status of this claim is requested.

3. Because this action raises new grounds of rejection, not necessitated by amendments to the claims, the action is being made Non-Final.

***Specification***

4. **(Prior Objection- Withdrawn)** The specification was objected to as failing to provide proper antecedent basis for the claimed subject matter. In view of the cancellation of this language from the claims, the objection is withdrawn.

5. **(New Objection)** The disclosure is objected to because of the following informalities: in the paragraph beginning on line 5 of page 13 ("Conservatively modified variations), several instances of the terms silent and conservatively appear to have typographical errors with the words being spelled as "Asilent" or "Aconservatively." Appropriate correction is required.

***Claim Objections***

6. **(Prior Objection- Withdrawn)** Claim 72 was objected to because of the following informalities: the word "the" was omitted from the last line of the claim. In view of the cancellation of the claim, the objection is withdrawn.

7. **(Prior Objection-Withdrawn)** Claim 72 was objected to in the prior action. In view of the cancellation of the claim, the objection is withdrawn as moot.

8. **(Prior Objection-Withdrawn)** Claim 72 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper

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dependent form, or rewrite the claim(s) in independent form. In view of the cancellation of the claim, the objection is withdrawn.

9. **(Prior Objection- Withdrawn)** Claim 78 was objected to because of the following informalities: no article was provided between the words "of" and "sequence." In view of the amendment to the claim, the objection is withdrawn.

10. **(New Objection)** Claim 71 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. This claim appears to read on a broader scope of inventions than the claim from which it depends. Claim 70, the independent claim, requires that the claimed antigenic peptide have one of SEQ ID NOs: 39, or 42-48. However, claim 71 appears to read on peptides that may have variants of these sequences, rather than the sequences themselves as required by claim 70. The claim therefore has a broader scope than the claim from which it depends.

***Claim Rejections - 35 USC § 112***

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. **(Prior Rejection-Withdrawn)** Claim 72 was rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and

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distinctly claim the subject matter which applicant regards as the invention. In view of the cancellation of this claim, and the new language in amended claim 70, the rejection is withdrawn.

13. **(Prior Rejection-Withdrawn)** Claim 78 was rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of the amendment of this claim, the rejection is withdrawn.

14. **(New Rejection-Necessitated by Amendment)** Claims 70, 71, 77, and 78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 70 is treated as representative of the rejected claims. This claim reads on a peptide comprising an antigenic determinant selected from SEQ ID NO: 39 or 42-48, wherein the peptide has an amino acid sequence selected from the group of SEQ ID NO: 11-72. The claim therefore specifies that the peptide have a sequence from one group of peptides and then further specifies that the peptide be selected from a larger group of sequences. It is therefore unclear what requirements the Applicant intends the claimed peptide to meet (i.e. the relationship of the claimed peptide to sequences from the two sequence groups is unclear). It is suggested that the phrase "wherein the antigenic peptide has an amino acid sequence selected from the group consisting of SEQ ID NOS: 11-72" be deleted from the claim.

For the purposes of this action, unless otherwise stated, the claims are being interpreted as reading on peptides selected from peptides comprising at least one sequence selected from the

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group consisting of SEQ ID NOs: 39, and 42-48, and wherein at least a portion of at least one of SEQ ID NOs: 38-42 is excluded.

15. **(New Rejection)** Claim 71 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim is rejected for two reasons. First, the claim is indefinite because it is unclear what is being claimed. Claim 71 reads on peptides with at least one substitution, addition, or deletion. However, the claim depends from claim 70, which requires the presence of at least one of SEQ ID NOs: 39, and 42-48. It is unclear whether the substitutions, deletions, or additions that alter the amino acid sequence are to be made within the claimed sequences, or if the variants are required to be outside of the antigenic determinant regions identified in claim 70.

The claim is also rejected because the phrase "a small percentage of amino acids" in the claim is a relative term, which renders the claim indefinite. The term "a small percentage" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. While the Applicant provides typical examples of what is meant by this term, there is no set definition by which one could determine the number of residues that may be altered in a given sequence.

Further, even if the specification had indicated what percent range of variations was permitted by a small percentage, no standard has been indicated as to what a small percentage of amino acids may be judged. I.e., it is not clear whether the small percentage would be

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determined by comparison of a particular variant peptide to a wild-type sequence corresponding thereto, by comparison of a variant sequence of SEQ ID NOs: 38, or 42-48 (as appropriate) to the disclosed sequences, or by comparison of the variation in the variant peptide to the sequence of the full length HAV P2A protein or polyprotein. The claim is therefore indefinite.

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. **(Prior Rejection- Withdrawn)** Claims 70-72 were rejected in the prior action under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antigenically reactive peptide consisting of one of SEQ ID NO: 38, or 42-46, does not reasonably provide enablement for any portion of the HAV polyprotein comprising one of these sequences. The rejection is withdrawn in view of Applicant's traversal, which was persuasive.

18. **(Prior Rejection-Withdrawn)** Claims 70-72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In view of the cancellation of claim 72, the rejection is withdrawn.

19. **(Prior Rejection-Withdrawn)** Claim 72 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies antigenic peptides comprising SEQ ID NO: 38, or 42-46 that bind antibodies that specifically bind one of SEQ ID NOs: 38, or



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42-46, does not reasonably provide enablement for any peptide according SEQ ID NOs: 11-72 that bind such an antibody. In view of the cancellation of this claim, the rejection is withdrawn.

20. **(New Rejection)** Claim 71 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This claim appears to read on HAV antigenic peptides comprising variants of the sequences of SEQ ID NOs: 39, and 42-48. However, while the Applicant indicates in the application that conservative variants may be made to the claimed peptide, the applicant has not provided any examples of substitutions, additions, or deletions, that may be made to the claimed sequences (other than of changing one sequence to another) without loss of anti-HAV antibody reactivity. Thus, the claims read broadly on any peptide comprising any variation to a small percentage of residues without guidance as to what variations may be made.

It is known in the art that the effects of amino acid substitution in a protein are unpredictable. See e.g., Bowie et al., Science 248: 1306-10, esp. page 1306 (teaching that while proteins are generally tolerant of amino acid substitutions, depending on the relationship of a particular residue to protein function and/or structure, a particular residue position may be extremely tolerant, may allow only conservative changes, or may not permit any substitutions). Further, the art also indicates that a single amino acid change may change a peptide/protein's ability to react with an antibody. See e.g., Riffkin et al., Gene 279-83 (teaching that a single amino acid change between two proteins was sufficient to create antigenically different proteins).

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See also, Mateu et al., J Gen Virol 71: 629-37 (1990). Thus, the art teaches that the effects of making changes to an amino acid sequence are unpredictable, and that such changes may, without further information than the sequence alone (e.g. essential residues), result in a change in the proteins ability to interact with a protein specific antibody. Because the Applicant has not demonstrated what residues may be substituted or otherwise changed in the claimed sequences, the Applicant is not enabled for peptide having any substitution, addition, or deletion.

***Claim Rejections - 35 USC § 102***

21. **(Prior Rejection- Withdrawn)** In the prior action, claims 70-72, 77, and 78 were rejected as anticipated under 35 U.S.C. 102(b) by Robertson et al., Journal of General Virology 73:1365-1377. The rejection is withdrawn in view of the amendments to the claims.

**(Prior Rejection-Withdrawn)** Claim 70 is rejected under 35 U.S.C. 102(b) as being anticipated by Jia et al., Journal of Infectious Diseases, 165:273-80 (1992- of record in the IDS filed on August 23, 2001). In view of the amendment to the claim, the rejection is withdrawn.

***Claim Rejections - 35 USC § 103***

22. **(Prior Rejection- Maintained)** Claims 70-72 were rejected in the prior action under 35 U.S.C. 103(a) as being obvious over Chiron Corp., EP 0199480. This rejection is withdrawn in view of the amendments to the claims.

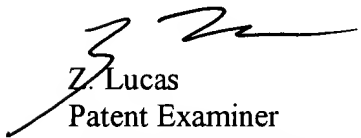
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***Conclusion***

23. Claims 83-89 appear to be allowable over the prior art.
24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

  
Z. Lucas  
Patent Examiner  
November 19, 2003

  
JAMES HOUSEL 12/1/03  
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